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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/804,481	03/12/2001	David de Graaf	WIBR-523-101	1227

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EXAMINER

STEELE, AMBER D

ART UNIT	PAPER NUMBER
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1639

MAIL DATE	DELIVERY MODE
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04/20/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.		Applicant(s)	
	09/804,481		GRAAF ET AL.	
	Examiner		Art Unit	
	AMBER D. STEELE		1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 February 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 32-35, 39-46 and 48-51 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 32-35, 39-46, and 48-51 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input checked="" type="checkbox"/> Other: <u>Notice to Comply; Defective CRF</u> . |

DETAILED ACTION

1. Please note: the examiner of record for the present application has changed. However, the Technology Center (TC1600) and Art Unit (AU1639) remain the same.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 9, 2009 has been entered.

Status of the Claims

3. The amendment to the claims received on February 9, 2009 canceled claims 1-31, 36-38, 47, and 52-53 and amended claims 32, 39, 42, and 49.

Claims 32-35, 39-46, and 48-51 are currently pending and under consideration.

Priority

4. The present application claims benefit of U.S. provisional application 60/188,304 filed March 10, 2000.

Sequence Compliance

5. Upon review of the application, it is noted that a defective CRF is present in the application history dated November 3, 2003. The defective CRF was not corrected. See the attached Notice to Comply. In addition, the sequence in Figure 4 requires a SEQ ID NO:.

Invention as Claimed

6. A recombinant vector comprising an isolated nucleotide sequence encoding an snRNA

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wherein the snRNA-encoding portion of said snRNA-encoding nucleotide sequence has been modified to contain a recognition site for a Type II dual cleavage restriction enzyme capable of cleaving said nucleotide sequence once upstream of said recognition site and once downstream of said recognition site such that digestion with a single said restriction enzyme excises from said vector a restriction fragment which includes said recognition site and forms insertion sites in said vector and variations thereof.

7. The presently claimed invention contains a process step (i.e. “excises from said vector a restriction fragment which includes said recognition site and forms insertion sites in said vector”) and functional limitations (i.e. capable of cleaving said nucleotide sequence once upstream of said recognition site and once downstream of said recognition site). See MPEP § 2113 and § 2173.05(g). Only the structure required by the presently claimed invention will be provided patentable weight (i.e. recombinant vector comprising an isolated nucleotide sequence encoding an snRNA wherein the snRNA-encoding portion of said snRNA-encoding nucleotide sequence has been modified to contain a recognition site for a Type II dual cleavage restriction enzyme).

Present claims 40-41 and 50-51 refer to the process step only. If applicants wish to claim the final product after the process step is completed, structural information regarding the final product must be incorporated into the claim language.

Withdrawn Rejections

8. The rejection of claims 32-35, 39-46, and 48-53 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

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application was filed, had possession of the claimed invention is withdrawn in view of the claim amendments received on February 9, 2009.

9. The rejection of claims 32-35, 39-46, and 48-53 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for Type II restriction enzymes wherein the cuts are made “outside” the recognition site, does not reasonably provide enablement for Type I/III and Type II wherein the cut is made inside the recognition site is withdrawn in view of the claim amendments received on February 9, 2009.

10. The rejection of claims 32-34, 37-46 and 48-51 under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Verhasselt et al. (Verhasselt et al., “Sequence Analysis of a 37.6 kbp Cosmid Clone from the Right Arm of *Saccharomyces cerevisiae* Chromosome XII” *Yeast* **1998**, *13*, 241–250) as evidenced by Sears et al. (Sears et al. “BaeI, another unusual BcgI-like restriction endonuclease” *Nucleic Acids Research* **1996**, *24*, 18, 3590-3592) and Genomenet (Genomenet, Database: EMBL-today Entry: X89514. Retrieved from http://www.genome.jp/dbget-bin/www_bget?embl-today+X89514 on 12/22/06, pages 1-17) is withdrawn in view of the claim amendments received on February 9, 2009.

11. The rejection of claims 32-35, 38-46 and 48-51 under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Shambaugh et al. (Shambaugh et al., “The splicesomal U small nuclear RNAs of *Ascaris lumbricoides*” *Molecular*

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and Biochemical Parasitology **1994**, 64, 349-352) as evidenced by Sears et al. (Sears et al. "BacI, another unusual BcgI-like restriction endonuclease" *Nucleic Acids Research* 1996, **24**, 18, 3590-3592) and NCBI (NCBI, Entry: L22246. Retrieved from <http://www.ncbi.nlm.nih.gov/entrez/viewer.fcgi?db=nucleotide&val=L22246> on 12/23/06, pages 1-3) is withdrawn in view of the claim amendments received on February 9, 2009.

New Rejections

Claim Rejections - 35 USC § 112

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 32-35, 39-46, and 48-51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a **new matter** rejection.

Various claim amendments were made to independent claims 32, 39, 42, and 49. However, applicants have neglected to specifically point out support for the claim amendments in the specification as originally filed. If applicants believe the claim amendments are not new matter, the applicants are respectfully requested to specifically point out support for the claim amendments in the specification as originally filed.

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 32-35, 39-46, and 48-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. One of skill in the art would not be able to determine the scope of the presently claimed invention. For example, the presently claimed vector refers to an intermediate vector while process limitations are present regarding the production of a final product. Therefore, it is not clear from the present claims if the intermediate vector or the final vector is required by the claims.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

17. Claims 32-35, 39-46, and 48-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Noonberg et al. U.S. Patent 5,624,803 issued April 29, 1997; Halle et al. U.S. 6,303,308 (effective filing date of May 10, 1999); and Abounader et al., Design and Expression of Chimeric U1/Ribozyme Transgenes, *Methods in Molecular Biology*, 252: 209-219.

For present claims 32-34, 39, 41-46, 48-49, and 51, Noonberg et al. teach vectors comprising a U6 snRNA promoter, a stabilizing region from which a hairpin-forming sequence can be transcribed, a nucleotide sequence of interest (wherein the sequence was inserted via the incorporation of two restriction enzyme cleavage sites), and a termination sequence wherein the stabilizing region is a sequence encoding a U6 snRNA hairpin region and the termination

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sequence is a sequence encoding a U6 snRNA (please refer to the entire specification particularly columns 8, 12-16, 18, 20-21; Examples 3-4; claims 1-3, 5, 16, 21-22, 24, and 26). In addition, Noonberg et al. teach that any restriction endonuclease can be utilized as long as two cleavage sites are present; any snRNA promoter, stabilizing region, and termination sequence can be utilized; and the sequence of interest can be between 10 and 60 nucleotides in length (please refer to the entire specification particularly columns 15-16, 18). Furthermore, Noonberg et al. teach a mutant U6 gene comprising only the first 6 and last 10 base pairs (see Example 3; Kunkel et al., Transcription of a human U6 small nuclear RNA gene *in vivo* withstands deletion of intragenic sequences but not of an upstream TATATA box, Nucleic Acids Research, 17(18): 7371-7379).

However, Noonberg et al. does not teach a Type II dual cleavage restriction enzyme particularly BaeI.

For present claims 32, 39-42, and 49-51, Halle et al. teach cloning vectors comprising BaeI (please refer to the entire specification particularly the abstract; columns 3 and 11; claims 1 and 13).

However, Noonberg et al. does not teach U1 snRNA.

For present claims 33-35 and 44-46, Abounader et al. teach a vector comprising a U1 snRNA chimeric transgene wherein the U1 snRNA loops flank an insert (please refer to the entire reference particularly the abstract; Figure 1; sections 2.2, 3.2).

The claims would have been obvious because the substitution of one known element (i.e. U6 snRNA and restriction enzymes taught by Noonberg et al.) for another (i.e. U1 snRNA taught by Abounader et al. and BaeI taught by Halle et al.) would have yielded predictable results (i.e.

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expression of either U6 or U1, restriction enzyme cleavage) to one of ordinary skill in the art at the time of the invention. See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AMBER D. STEELE whose telephone number is (571)272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amber D. Steele/
Primary Examiner, Art Unit 1639

April 15, 2009